mimic the inhibitory activity of the soluble peptide analogs.

2. Determine the mechanism of the Tat peptide inhibition.

3. Establish a suitable non-invasive peptide delivery system for the preclinical and animal model studies.

4. Determine the effective dose of Tat peptide analogs in combination with other anti-retroviral drugs.

5. Determine the stability, half-life, and distribution of the Tat peptides upon delivery into cells.

6. Conduct *in vivo* testing of appropriate compounds and/or peptide analogs.

7. Evaluate *in vivo* test results.

8. Develop vehicle for delivery of compounds to patients.

9. Conduct pre-clinical and clinical trials of appropriate candidate compounds and/or peptide analogs.

10. Prepare manuscripts for publication.

Criteria for choosing the collaborator include its demonstrated experience and commitment to the following:

1. The aggressiveness of the development plan, including the appropriateness of milestones and deadlines for preclinical and clinical development.

2. Scientific expertise in and demonstrated commitment to the development of drug delivery systems.

3. Experience in preclinical and clinical drug development.

4. Experience and ability to produce, package, market and distribute pharmaceutical products.

5. Experience in the monitoring, evaluation and interpretation of the data from investigational agent clinical studies under an IND.

6. A willingness to cooperate with the NCI and FDA in the collection, evaluation, publication and maintaining of data from pre-clinical studies and clinical trials regarding the subject compounds.

7. Provision of defined financial and personnel support for the CRADA to be mutually agreed upon.

8. An agreement to be bound by the DHHS rules involving human and animal subjects.

9. Scientific expertise in and demonstrated commitment to the treatment of HIV infection and related disorders.

10. Provisions for equitable distribution of patent rights to any CRADA inventions. Generally the rights of ownership are retained by the organization which is the employer of the inventor, with (1) an irrevocable, nonexclusive, royalty-free license to the Government and (2) an option for the collaborator to elect an exclusive or nonexclusive license to Government owned rights under terms that comply with the appropriate licensing statutes and regulations.

Dated: November 12, 1996.

Kathleen Sybert,

Deputy Director, Office of Technology Development, OD, NCI.

[FR Doc. 96–29892 Filed 11–21–96; 8:45 am]

BILLING CODE 4140–01–M

Government-Owned Inventions; Availability for Licensing

AGENCY: National Institutes of Health, Public Health Service, DHHS.

ACTION: Notice.

SUMMARY: The inventions listed below are owned by an agency of the U.S. Government and are available for licensing in the U.S. in accordance with 35 U.S.C. 207 to achieve expeditious commercialization of results of federally-funded research and development.

ADDRESSES: Licensing information and a copy of the U.S. patent applications referenced below may be obtained by contacting Joseph Contrera, M.S., J.D., at the Office of Technology Transfer, National Institutes of Health, 6011 Executive Boulevard, Suite 325, Rockville, Maryland 20852–3804 (telephone 301/496–7056 ext 244; fax 301/402–0220). A signed Confidential Disclosure Agreement will be required to receive a copy of the patent applications.

A Novel Vector for Polynucleotide Vaccines

EL Nelson, PJ Nelson (NCI)
Serial No. 60/023,931 filed 14 Aug 96

This invention is directed to a ''humanized'' polynucleotide vector vaccine which uses covalent closed circular (CCC) plasmid DNA, ''naked DNA,'' to express target antigens. The vector contains the necessary elements to express mRNA for a target antigen. The plasmids are non-replicating but are capable of extended stable expression of the target sequences in skeletal muscle and professional antigen presenting cells generating an immune response to the target antigen in immunized individuals. The polynucleotide vector is particularly useful in accommodating monomorphic and polymorphic tumor antigens via PCR technology. This invention could be useful in constructing polynucleotide vector cancer vaccines or ''naked DNA'' vaccines containing one or more tumor antigens.

Heterologous Boosting Immunizations for the Generation of CTL and Anti-Tumor Responses

RS Chamberlain, KR Irvine, SA Rosenberg, NP Restifo (NCI)
Serial No. 60/015,893 filed 22 Apr 96

A number of recombinant and synthetic vectors expressing tumor associated antigens have been developed which each induce powerful cellular and humoral immune responses that correlated with anti-tumor immunity in murine tumor model systems. Examples of these vectors include (1) recombinant viruses, such as vaccinia, fowlpox and adenovirus, (2) recombinant plasmid DNA, and (3) minimal determinant peptides. This invention involves the use of more than one of these vectors expressing a particular antigen for priming and boosting immunization regimens with the goal of enhancing anti-tumor immunity. Boosting with heterologous vectors induced more powerful primary antigen-specific cytotoxic T lymphocyte responses than boosting with the same vector. These more powerful immune responses induced by subsequent immunization with a different vector than the priming agent also resulted in a significant prolongation in survival of tumor-bearing mice as compared to mice that received two vaccinations with the same vector. Specifically, the combinations that were most efficacious were recombinant vaccinia virus followed by recombinant fowlpox and vice versa and recombinant DNA immunization followed by either recombinant fowlpox or vaccinia virus and vice versa.

The invention is significant because these heterologous boosting strategies may provide for increased therapeutic potential in the design and development of immunotherapies for cancer treatment. This approach may also be useful in the development of treatments for infectious bacterial and viral disease.

Point Mutated ras Peptides for the Generation of CD8+ Cytotoxic T Lymphocytes

J. Schlom, S Abrams (NCI)
Serial No. 08/635,344 filed 19 Apr 96

This invention is directed to a method of inducing a cytotoxic T cell response where the cytotoxic T cells are $CD8^+$ T cells. The $CD8^+$ cytotoxic T cell response is induced by peptides which contain a mutation in the K-*ras* oncogene at codon 12. The invention discloses 13 mer K-*ras* peptides spanning position 5–17 of the K-*ras* gene and which contain a mutation at codon 12. In addition, 9 mer and 10 mer K-*ras* peptides are also described in

which they both span codon 12 and in which codon 12 is mutated. This invention could be useful in cancer vaccines and adoptive immunotherapy.

Dated: November 13, 1996.

Barbara M. McGarey,

Deputy Director, Office of Technology Transfer.

[FR Doc. 96–29893 Filed 11–21–96; 8:45 am]

BILLING CODE 4140–01–M

Government-Owned Inventions; Availability for Licensing

AGENCY: National Institutes of Health, HHS.

ACTION: Notice.

The inventions listed below are owned by agencies of the U.S. Government and are available for licensing in the U.S. in accordance with 35 U.S.C. 207 to achieve expeditious commercialization of results of federally funded research and development. Foreign patent applications are filed on selected inventions to extend market coverage for U.S. companies and may also be available for licensing.

ADDRESSES: Licensing information and copies of the U.S. patent applications listed below may be obtained by writing to the indicated licensing contact at the Office of Technology Transfer, National Institutes of Health, 6011 Executive Boulevard, Suite 325, Rockville, Maryland 20852–3804 (telephone 301/496–7057; fax 301/402–0220). A signed Confidential Disclosure Agreement will be required to receive copies of the patent applications.

Production of Infectious Respiratory Syncytial Virus From Cloned Nucleotide Sequences

PL Collins (NIAID)
Serial No. 08/720,132 filed 27 Sep 96 (claiming priority date of 27 Sep 95)
Licensing Contact: Robert Benson, 301/496–7056 ext 267

This invention is a method of producing infectious RSV from cDNA encoding the RSV relicative intermediate RNA and cDNA encoding the N, P, L and M2(ORF1) proteins of RSV, which are used to transfect a cell. Claimed are cells or cell lysates comprising these cDNA molecules, recombinant RSV and methods of producing the recombinant RSV. The invention is particularly useful for producing mutant RSV as attenuated RSV vaccine candidates. Mutations in the RSV genome known to have an attenuated phenotype can be placed together in the RSV genome using known techniques and made into infections in the RSV genome using known techniques and made into infectious RSV using the invention. Vaccine candidates can be stably stored as cDNA molecules and modified as needed, for example to accommodate genetic drift in circulating RSV. The invention is described in P.N.A.S. *92*, 11563–11567, 1995. This patent application has been foreign filed. (portfolio: Infectious Diseases-Vaccines, viral, non-AIDS; Infectious Diseases-Research Materials)

Glycoprotein Hormone Superagonists

MW Szkudlinski, BD Weintraub, M Grossman (NIDDK)
OTT Reference No. E–015–96/0 filed 08 May 96
Licensing Contact: J. Peter Kim, 301/496–7056 ext 264

The glycoprotein hormones, which include thyroid-stimulating hormone, follicle-stimulating hormone, luteinizing hormone, and chorionic gonadotropin, are involved in the development and regulation of the ovary, testes, and thyroid. These hormones are heterodimers, each consisting of a non-covalently linked alpha and beta subunit. While the amino acid sequence of the beta subunit is hormone-specific, that of the alpha subunit is identical in all hormones within the same species. Embodied in the current invention are human glycoprotein hormones which contain specific amino acid substitutions within the alpha as well as beta subunits. These substitutions result in glycoprotein hormone analogs, or ''superagonists,'' which exhibit a significant increase in in vitro and in vivo bioactivity over the wild-type hormone. These superagonists, therefore, appear to represent potential agents for use in the treatment of a variety of conditions, including various forms of male and female infertility and thyroid carcinoma. (portfolios: Internal Medicine-Therapeutics, contraceptives; Internal Medicine-Other)

Inhibitory and Non-Inhibitory Antigen Binding Polypeptides Against Human P450 Enzymes

HV Gelboin, FJ Gonzalez (NCI)
Serial No. 08/559, 808 filed 17 Nov 95
Licensing Contact: Leopold J. Luberecki, Jr., 301/496–7735 ext 223

This invention concerns monoclonal antibodies (MAbs) specific for particular members of the cytochrome P450 family of enzymes. The cytochrome P450s are the metabolic interface between xenobiotics and their metabolism in human and other species as well as for the metabolism of endobiotics. A large array of drugs, mutagens, carcinogens, pesticides, environmental chemicals, fatty acids, bile acids, and steroids are metabolized by individual forms of cytochrome P450. The invention involves the construction, isolation, and production of MAbs that specifically bind to human cytochrome P450 3A3, 3A4, 3A5, and 2E1 and that specifically inhibit the enzyme activity of human cytochrome P450 3A3, 3A4, and 3A5, and 2E1 (inhibitory MAbs) and MAbs that specifically bind to cytochrome P450 3A3, 3A4, 3A5, and 2E1, without inhibiting enzyme activity (non-inhibitory MAbs). Novel inhibitory MAbs to human P450 have been in development for some time. These MAbs can be used to assess adverse reactions in patients to compounds and to identify populations that would exhibit different sensitivities to the therapeutic or toxic effects of compounds. Cytochrome P450 3A4 and 3A3 are very important members of the P450 family of enzymes. The human P450 3A4 and 3A3 metabolize a large variety of drugs, steroids, and carcinogens. Cytochromes P450 3A3 and 3A4 are considered the most important P450s for a wide range of high molecular weight substrates which include many of the known clinically useful drugs, such as tranquilizers, antidepressants, immunosuppressants, and anticancer drugs. Cytochrome P450 2E1 is important because it metabolizes low molecular weight compounds susceptible to environmental hazards and carcinogens. The human P450 2E1 also metabolizes clinically useful drugs such as the anesthetic chlorzoxazone and the analgesic acetaminophen as well as caffeine. Issuance of a patent for this invention is currently pending. (portfolio: Internal Medicine-Miscellaneous; Cancer-Research Reagents, MAb based; Internal Medicine-Diagnostics; Cancer-Diagnostics, in vitro, MAb based)

Prevention of Progression in Vascular Disease

GE Striker, LJ Striker, FP Sherman (NIDDK)
Serial No. 08/478,347 filed 07 Jun 95
Licensing Contact: Carol Lavrich, 301/496–7056 ext 287

This invention relates to efficacious methods and pharmaceutical compositions in the treatment of chronic progressive vascular diseases (CPVD) characterized by scarring and/or fibrosis to halt and reverse the disease process by resolving scar and fibrotic lesions. These methods consist of the administration to patients of an effective amount of Elmiron. The oral route of administration is preferred, with total